

WHAT IS CLAIMED IS:

1. A method of screening a mixture for active entities, which method comprises:
 - (i) providing a plurality of ligands, wherein each ligand is attached to a support to form a plurality of ligand-support complexes,
 - (ii) contacting the ligand-support complexes with a mixture comprising a plurality of entities under conditions that allow at least one entity to bind to at least one ligand-support complex, thereby forming at least one entity-ligand-support complex,
 - (iii) separating at least one entity-ligand-support complex from the unbound entities,
 - (iv) assaying at least one entity of at least one separated entity-ligand-support complex for an activity,
 - (v) detecting the activity, and
 - (vi) selecting at least one entity-ligand-support-complex having the entity, which exhibited the detected activity,whereupon a mixture is screened for active entities.
2. The method of claim 1, wherein the ligands are selected from the group consisting of cells, bacteria, viruses, yeast, proteins, peptides, amino acids, nucleic acids, carbohydrates, lipids, drugs, synthetic inorganic compounds, synthetic organic compounds, isoforms of any of the foregoing, and combinations of any of the foregoing.
3. The method of claim 2, wherein the ligands are peptides, and the peptides are generated by combinatorial approaches.
4. The method of claim 1, wherein the support comprises a material selected from the group consisting of polymethacrylates, polyacrylates, agarose, polyacrylamides, dextran, cellulose, polysaccharides, nitrocellulose, silicon, styrene, polyethylene-coated polystyrene, metal, polyvinylidifluoride, nylon, and combinations of any of the foregoing.
5. The method of claim 1, wherein the mixture is a biological fluid, an environmental extract, or a composition comprising chemical compounds.
6. The method of claim 5, wherein the biological fluid is selected from the group consisting of blood, plasma, pooled plasma, intermediates from plasma fractionation, serum, a cell homogenate, a tissue homogenate, a conditioned medium, a fermentation broth,

cerebrospinal fluid, urine, saliva, milk, ductal fluid, tears, perspiration, lymph, semen, umbilical cord fluid, and amniotic fluid.

7. The method of claim 5, wherein the biological fluid is a plasma-derived fraction comprising antibodies and anti-idiotypic antibodies.

8. The method of claim 5, wherein the biological fluid is obtained from a host afflicted with a disease.

9. The method of claim 5, wherein the environmental extract is selected from the group consisting of a soil extract, an extract from a naturally-occurring body of water, a sample of ice, air, ash, rock, or permafrost, and a swab from a building.

10. The method of claim 5, wherein the composition comprising chemical compounds comprises natural or synthetic chemical compounds.

11. The method of claim 1, wherein the entities are selected from the group consisting of proteins, peptides, drugs, antibodies, cells, synthetic molecules, organic compounds, protein complexes, bacteria, viruses, and fungi.

12. The method of claim 1, wherein the activity is a biological, physical, chemical, or biochemical activity.

13. The method of claim 12, wherein the activity is an enzyme activity or inhibition of an enzyme activity.

14. The method of claim 12, wherein the activity is an effect on a cell, a cell population, a tissue, or a whole organism.

15. The method of claim 14, wherein the activity is an effect on a cell or a cell population and the effect is selected from the group consisting of cell migration, cell proliferation, cell death, cell differentiation, cell cycle entry, cell cycle arrest, apoptosis, cell lysis, growth arrest, cell survival, a change in an intracellular signaling pathway, antigen expression, gene upregulation, gene downregulation, and a phenotypic change in response to an agent.

16. The method of claim 14, wherein the cell, cell population, tissue, or whole organism is diseased.

17. The method of claim 16, wherein the diseased cell, cell population, tissue, or whole organism is diseased with cancer, diabetes, an autoimmune disease, osteoporosis, or lung disease, infected with a parasite, virus, or bacteria, wounded, burned, scarred, or in a state of healing.

18. The method of claim 1, wherein multiple entity-ligand-support complexes are formed in step (ii).

19. The method of claim 1, which further comprises, after step (iii) and before step (iv), a sub-pooling step, wherein at least one separated entity-ligand-support complex and the ligand-support complexes are separated into several pools.

20. The method of claim 1, which further comprises (vii) determining the chemical identity of at least one ligand to which at least one entity exhibiting the detected activity binds.

21. The method of claim 20, which further comprises
(viii) providing multiple copies of at least one ligand identified in step (vii),
(ix) attaching each copy to a support, thereby obtaining multiple ligand-support complexes,
(x) contacting the ligand-support complexes with a composition comprising multiple copies of at least one entity exhibiting the detected activity under conditions that allow the ligand-support complexes to bind to multiple copies of at least one entity exhibiting the detected activity, thereby forming multiple entity-ligand-support complexes, and
(xi) dissociating the entities from the entity-ligand-support complexes, thereby recovering the entities from the composition.

22. The method of claim 21, wherein the composition of step (x) is the same as the mixture of step (ii).

23. The method of claim 21, which further comprises
(xii) determining the chemical or physical identity of the entity exhibiting the detected activity.

24. The method of claim 19, which further comprises, after the sub-pooling step and before step (iv), an eluting step, wherein the entities of the multiple entity-ligand-support complexes are dissociated from the complexes, and the ligand-support complexes are subsequently removed from the pools.

25. The method of claim 19, which method comprises, after the sub-pooling step and before step (iv), a step, wherein a semi-solid or viscous material is added to each pool, wherein the entity of at least one entity-ligand-support complex dissociates from the complex and diffuses into the material, thereby forming a concentration gradient of the entity, wherein the concentration of the entity gradually decreases as the distance from the ligand-support complex from which the entity dissociated increases.

26. A method of screening a mixture for active entities, which method comprises:

- (i) providing a plurality of ligands, wherein each ligand is attached to a support to form a plurality of ligand-support complexes,
 - (ii) contacting the ligand-support complexes with a mixture comprising a plurality of entities under conditions that allow at least one entity to bind to at least one ligand-support complex, thereby forming at least one entity-ligand-support complex,
 - (iii) separating at least one entity-ligand-support complex and the ligand-support complexes from the unbound entities,
 - (iv) separating at least one entity-ligand-support complex and the ligand-support complexes into pools,
 - (v) dissociating at least one entity from at least one separated entity-ligand-support complex,
 - (vi) removing from the pools the ligand-support complexes or the at least one dissociated entity of step (v),
 - (vii) assaying at least one dissociated entity of step (v) for an activity,
 - (viii) detecting the activity, and
 - (ix) selecting at least one entity exhibiting the detected activity,
- whereupon a mixture is screened for active entities.

27. A method of screening a mixture for active entities, which method comprises:

- (i) providing a plurality of ligands, wherein each ligand is attached to a support to form a plurality of ligand-support complexes,

- (ii) contacting the ligand-support complexes with a mixture comprising a plurality of entities under conditions that allow at least one entity to bind to at least one ligand-support complex, thereby forming at least one entity-ligand-support complex,
 - (iii) separating at least one entity-ligand-support complex and the ligand-support complexes from the unbound entities,
 - (iv) separating at least one entity-ligand-support complex and the ligand-support complexes into pools,
 - (v) adding a semi-solid or viscous material to each pool, wherein the entity of the at least one separated entity-ligand-support complex dissociates from the complex and diffuses into the material, thereby forming a concentration gradient of the entity, wherein the concentration of the entity gradually decreases as the distance from the ligand-support complex from which the entity dissociated increases,
 - (vi) assaying at least one dissociated entity of step (v) for an activity,
 - (vii) detecting the activity, and
 - (viii) selecting at least one entity exhibiting the detected activity,
- whereupon a mixture is screened for active entities.